

nological advances is limitless and will revolutionize the future of disease identification, monitoring, and treatment based on the experiences of connected individuals.

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Biotin Interference in Diagnostic Tests

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Despite sobering evidence of no benefit or even possible harm, the use of vitamin and mineral supplements by adults continues to grow. It is estimated that the US supplement industry is now costing consumers over \$30 billion annually. Laboratorians have long had to contend with potential analytical interferences due to ingested substances. Now, biotin has become a pervasive interferent, increasingly insidious and problematic to clinical laboratory testing.

Biotin, also known as vitamin B7, is an essential coenzyme involved in carbon dioxide transfer in carboxylase reactions. The US Department of Agriculture–recommended Dietary Reference Intake (DRI)² of biotin is 30 μg per day and supplementation is normally not necessary as biotin is ubiquitous in common foods. However, for the past several years, biotin has been marketed as a beauty supplement. One label on a biotin bottle reads, “For lustrous hair, radiant skin, and strong nails.” Although these beauty claims are not well supported, biotin’s popularity is at an all-time high due to heavy marketing and receptive consumers. Because over-the-counter biotin is not regulated and is sold as a beauty product, there are no records of the actual amounts that are being ingested, but many tablets contain upwards of 10 mg, suggesting that consumers are taking amounts of biotin far in excess of the DRI. The only medical evidence in support of megadoses of biotin (up to 300 mg per day, 10 000 times the DRI) applies to patients

with secondary progressive multiple sclerosis, in whom clinical symptoms and quality of life have been improved by using biotin as a complementary medicine. High doses of biotin (5–30 mg per day) may also be indicated for rare metabolic disorders such as biotinidase deficiency and propionic acidemia.

Even in large doses, biotin is considered nontoxic and is unlikely to cause any side effects. The potential medical issue is that a large amount of biotin in a patient’s sample can interfere with a broad range of diagnostic tests. Specifically, serum or plasma biotin may potentially impact any assay that uses biotin–streptavidin binding (1). Owing to streptavidin’s extraordinarily high affinity for biotin [dissociation constant (K_d) of 10^{-14} mol/L] and binding under a wide variety of chemical conditions, biotin–streptavidin is a popular component of assay architecture for many molecular tests and immunoassay platforms.

Unfortunately, susceptibility to biotin interference is variable in magnitude and can skew results to be either falsely high or falsely low depending on the assay design and conditions. The ramifications for patients and caregivers are potentially grave. In typical competitive immunoassays for small molecules such as free thyroxine (fT4), free triiodothyronine (fT3), testosterone, estradiol, and cortisol, biotin interference blocks assay signal. Because signal is inversely proportional to analyte concentration in competitive assays, biotin can cause falsely high results. In the 2-site “sandwich” immunoassay format [typical for larger protein analytes such as thyroid-stimulating hormone (TSH), thyroglobulin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), insulin, and for autoantibodies], excess biotin competes with the biotinylated complex causing a reduction in signal and a falsely lower result. This combination of 2 types of biotin interference can create the perfect factitious biochemical evidence of Graves thyrotoxicosis with highly increased

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² Nonstandard abbreviations: DRI, dietary reference intake; K_d , dissociation constant; fT4, free thyroxine; fT3, free triiodothyronine; TSH, thyroid-stimulating hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone.

fT₄ and fT₃, positive TSH receptor antibodies and suppressed TSH. Similar scenarios of biotin interference can be imagined for extremely high steroid hormone concentrations with suppressed LH or FSH, which would be suggestive of tumors.

A broad range of laboratory tests beyond endocrine assays may be impacted similarly by biotin-induced interference, which can give rise to either very confusing results or very compelling factitious results. Extreme laboratory test values as well as clinically discordant ones may be easily recognized as interferences, but subtle or moderate biotin-induced changes in results would not be identifiable by the laboratory. Even a slight skewing of results can pose serious ramifications for tests in which misdiagnosis of serious infectious diseases such as HIV or hepatitis C virus or failure to recognize a tumor recurrence may occur. Emergency room patients may be at risk if biotin interferes with the assays for cardiac markers. Patients on thyroid medication may be titrated improperly owing to inaccurate but clinically congruous laboratory results. And the list goes on, and clinicians who recognize these problems will be looking to laboratorians for guidance.

While biotin interference in immunoassays has been known for years, it was a rare problem until biotin megadoses recently became commonplace. The ideal solution is to fix the biotin interference analytically, but this is a costly and a long-term proposition. Possible solutions may require removal of biotin in the assay design by pretreating samples with streptavidin or by adding biotin extraction steps. Such modifications will require extensive revalidation to demonstrate that performance is not affected. For now, laboratorians should become familiar with the availability of alternative assays that are free of

biotin–streptavidin components to allow troubleshooting of discrepant results.

The practical and immediate solution to prevent or at least limit biotin interference will be to increase clinician and patient awareness of biotin's effects on tests. Physicians and other practitioners should inquire and advise patients to abstain from biotin intake for a few days before blood draw. This counsel is necessary although biotin has a very rapid elimination half-life of about 2 h; theoretically, most of it should clear from the body within 4–5 h. However, pharmacokinetic studies of a patient ingesting megadoses (30 mg) of biotin revealed that its interfering effects on laboratory tests persisted for up to 24 h. For patients on megadoses of biotin, this finding means that it is prudent to stop taking biotin for at least 2 days before blood draws.

With biotin use being so pervasive, it is critical that laboratorians and clinicians are aware of biotin interference so that misdiagnosis and inappropriate treatment can be prevented.

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A Setback to Universal Pediatric Lipid Screening and a Call for More Research

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In 2011, a report published by the National Heart, Lung, and Blood Institute on pediatric cardiovascular health

and risk reduction put forth a recommendation for universal lipid screening in children and adolescents between the ages of 9 and 11 (1). Although the American Acad-

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